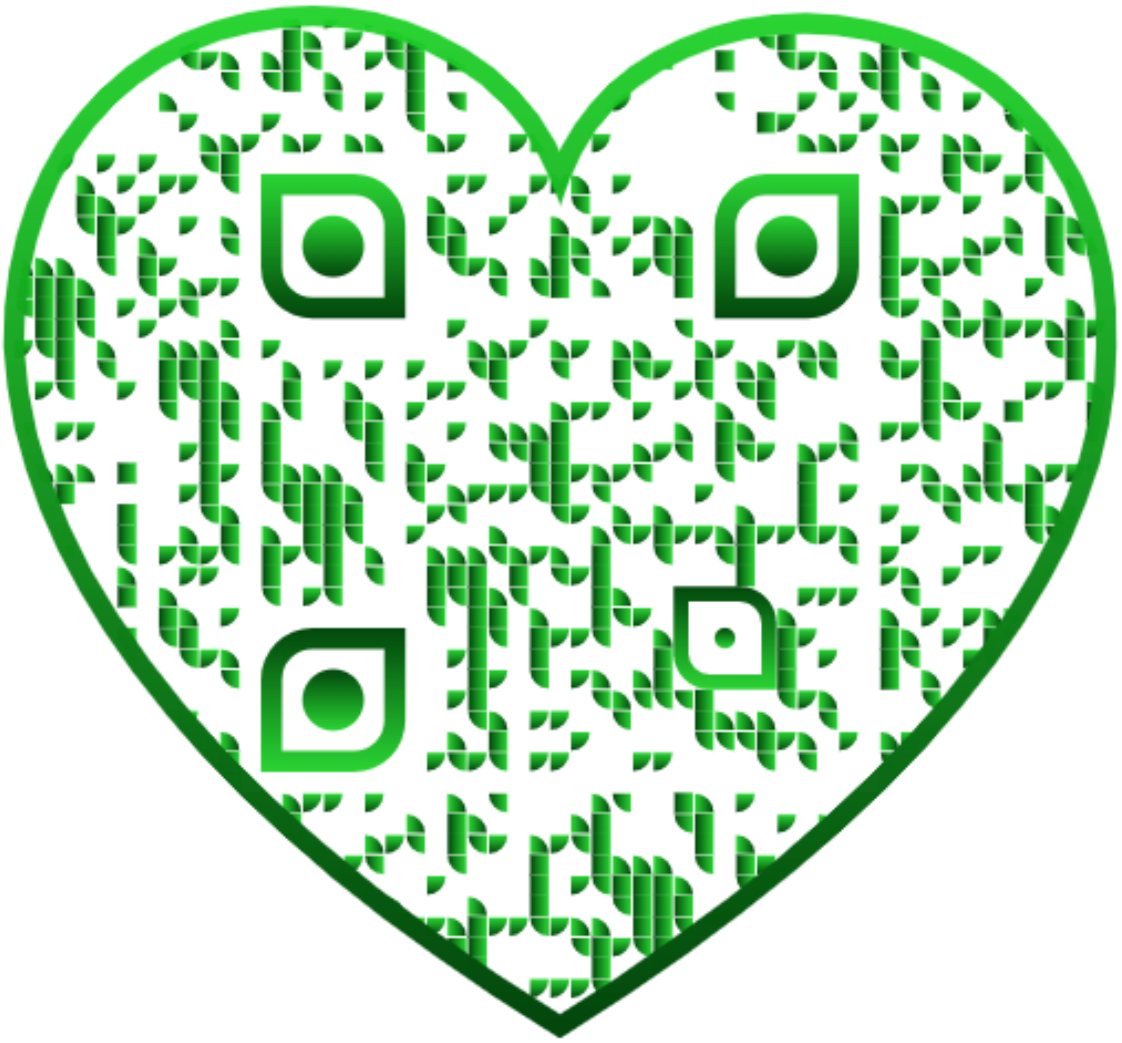
Chapter Eight
Assessing Articles and Critique of Pharmacoeconomic Studies



1. Strategies for applying Pharmacoeconomics
2. Assessing Articles and Critique of Pharmacoeconomic Evaluation
3. Markov Models of Chronic Conditions

Strategies for applying pharmacoeconomics

At the end of this sections, students will be able to

- Identify strategies for applying pharmacoeconomics to assess the value of pharmaceutical products and services
- Differentiate among strategies and when to use the strategies
- Apply Strategies to do pharmacoeconomcis decisions.

Strategies to Incorporate PE into Pharmacotherapy

- Various strategies are available to incorporate PE into pharmacotherapy.
- Popular strategies for applying pharmacoeconomics to assess the value of pharmaceutical products and services include:
  1) Using the results of published pharmacoeconomic studies
  2) Building economic models and
  3) Conducting local pharmacoeconomic research

1) Use the Pharmacoeconomic Literature

- Many pharmacoeconomic analyses are published in primary medical and pharmacy literature sources
- To use this literature as an aid in decision making, it must be:
  - critically evaluated for quality and rigor and
  - interpreted correctly
- Therefore, prior to using pharmacoeconomic data to make clinical and policy decisions, decision makers should recognize the potential limitations of those data.

- A primary consideration when evaluating and interpreting a study is the ability to generalize or transfer the results to other healthcare settings and countries
- It can be difficult to generalize and transfer the results of a published study, primarily because of:
  - wide variations in practice patterns
  - patient populations, and
  - costs among healthcare systems and countries
- These and other factors present a challenge for practitioners attempting to extrapolate or relate exact cost savings or cost ratios to their own practice settings

- To enhance the ability to use pharmacoeconomic results published in the literature, consider the following points:
  - What is the technical merit of the study?
  - Are the results applicable to local decision making?
  - Do the results apply generally in different jurisdictions with different perspectives?
- Various guidelines, criteria, reviews, and consensus-based recommendations for evaluating, conducting, and reporting pharmacoeconomic literature have been published

(2) Build an Economic Model

- Modeling studies use existing clinical and/or epidemiologic data to project future outcomes
- Use of economic models can provide support for various clinical decisions, especially those which are time-contingent
- Identifying assumptions regarding the treatment alternatives being compared, the patient outcomes under study, and the probability of those outcomes occurring can provide the basis for an economic simulation to assist in the medication decision-making process

- Using an economic model can help the clinician to forecast the impact of medication-use decisions on a patient, institution, or healthcare system.
- Also, as new drugs are marketed that can displace older agents, an economic model can expedite the reappraisal process for formulary management and drug-use policy decisions
- When building an economic model to assist in clinical decision making, various published studies and a review can be considered.
- Typically, economic modeling in today's practice settings employs clinical decision analysis, which has been defined as an explicit, quantitative, and prescriptive approach to choosing among alternative outcomes.

(3) Conduct Local Pharmacoeconomic Evaluation

- Clinicians may need to conduct a pharmacoeconomic evaluation if:
  - There is insufficient literature
  - Published results cannot be extrapolated to clinical practice or
  - Building a model is not appropriate
- Before conducting a pharmacoeconomic evaluation, clinicians should be familiar with the similarities, differences, and appropriate application of pharmacoeconomic methods. *(Discussed in chapters 5,6,7)*

- Conducting local pharmacoeconomic evaluations consumes both time and monetary resources

- Therefore, specific pharmacy products and services for pharmacoeconomic evaluation should be targeted

- Thus this strategy should be reserved for pharmacy decisions that may have a significant impact on cost and/or quality of care

Assessing Articles and Critique of Pharmacoeconomic Evaluation

Section Objective

Upon completing this section, the reader will be able to:

1. List and understand 14 questions to consider when reviewing a PE research article
2. Examples and explanations of 14 questions to consider when reviewing a PE research article
3. Apply the criticism and evaluate PE research articles

Critiquing Research Articles

- There is no one standard, agreed-upon method used to conduct a PE analysis. However, there are many acceptable methods.
- Appropriateness of these methods depends on many factors, including
  - Specific question or objective,
  - Perspective of the study,
  - time period needed to determine outcomes of the alternatives, and the resources (e.g., time, money, databases) available to researchers.
- No study is perfect; thoroughness is balanced with the practicality of the research. However, several authors do cite methodology to assist in systematically reviewing the pharmacoeconomic.
- 14 questions illustrate the types of questions that should be raised when reviewing pharmacoeconomic studies.

1. Complete Title: Is the Title Appropriate?

- From reading the title, can it be determined what is being compared and what type of study is being conducted— CEA, CUA, CBA, or a combination.
- Example, a title “Pharmacoeconomic Analysis of Glipizide versus Glyburide in the Veterans Administration” does not specify the type of study (CMA, CEA, CBA, or CUA) conducted.
- Although this is not wrong, readers may prefer to know what type of study was conducted when searching for articles that are relevant to their purpose.
- The title is vague about what is being compared.
- Example, the title “CEA of Two Antibiotic Therapies in a Large Teaching Hospital” does indicate the type of study that was conducted but not the alternatives that were compared.
- In some cases, the title itself may seem biased. For example, a title (here using names of medications that do not exist) such as Ultraceph Found Cost-Effective When Compared to Megacephsounds like advertising rather than a scientific-based research..

2. Clear Objective: Is a Clear Objective Stated?

- Was a well-defined question posed in an answerable form? This should be clearly stated at the beginning of the article.
- Example of clear objectives might be "The objective of this study was to calculate the benefit-to-cost ratio of pharmacist interventions in our hospital." or
- Example 2: "Our purpose was to perform an incremental cost utility analysis of standard chemotherapy compared with palliative treatment alone for patients with inoperable lung cancer."
- An example of an unclear statement would be "The objective of our study is to determine if Ultraceph is better than Megaceph." This statement leaves the reader wondering better in what way?

3. Appropriate Alternatives: Were Appropriate Alternatives or Comparators Considered?

- Ideally, the most effective treatments or alternatives should be compared.
- In pharmacotherapy evaluations, the manufacturers of innovative new products often compare or measure the new product against a standard current therapy.
- If a new treatment option is being considered, comparing it with an outdated treatment or a treatment with low efficacy rate is a waste of time and money.
- A new treatment should be compared with the next best alternative or the alternative it may replace. Alternatives may include drug treatments and nondrug treatments (e.g., medication versus surgery).
- Head-to-head comparisons of the best alternatives provide more information than comparisons of a new product or service with an outdated or ineffective alternative.
- In many CBAs, the options may be thought of as a "with or without" option. The comparison of a service or a preventative therapy (e.g., a vaccination or immunization) is compared with the alternative of not implementing the service or providing the preventative therapy.

4. Alternatives Described: Was a Comprehensive Description of the Competing Alternatives Given?

- If pharmaceutical products compared, the dosages and length of therapy should be included.
- Don't compare a low dose of one drug with a high dose of a competing drug. range of doses may given based on the range given to a specific population of patients.
- In chemotherapy research, sometimes researchers describe the doses as "equitoxic"—a dose based on the amount a patient can tolerate without severe side effects— because patients need to be individually dosed based on their body mass index, their immunity status, and their reactions to the medication.
- If pharmacy services are compared, explicit details of the services make the paper more useful. For these services, a description of start-up and continuing resource needs should be addressed, if applicable. For example, additional training for pharmacists and other health care professionals and space, overhead, equipment, or software needs may be required to provide the service.
- A summary of the services provided should be outlined. For example, if a pharmacist in a diabetes clinic provides services, readers would want to know how patients are identified, what topics are covered with the patient, and what type of follow-up is provided. A large part of the expense of providing pharmacy services may be personnel costs.

5. Perspective Stated: Is the Perspective of the Study Addressed?

- It is important to identify from whose perspective the analysis will be conducted because this determines the costs to be evaluated.
- Is the analysis being conducted from the perspective of the patient, hospital, clinic, insurance company, or society?
- Depending on the perspective assigned to the analysis, different results and recommendations based on those results may be identified.
- Some articles are not clear about what type of costs or whose costs is used in the calculations, and it is up to the reader to guess the perspective.
- In more recent articles, editors and reviewers are more aware that readers look for a sentence that explicitly states, "The perspective of the study was. . ." Some articles may use acceptable phrases such as "total third-party reimbursements for prescription and medical services were measured and summed"

6. Type of Study: Is the Type of Study Stated?

- Knowing up front the type of pharmacoeconomic study that is being conducted helps readers follow the rest of the research article.
- As mentioned, it is helpful if the type of study is mentioned in the title. Some articles contain more than one type of study.
- For example, an article comparing chemotherapy options may include both cost-effectiveness calculations (cost per year of life saved) and cost-utility calculations (cost per quality-adjusted life year) and may compare the results of both.

7. Relevant Costs: Were All the Important and Relevant Costs Included?

- Based on the stated perspective, were the appropriate types of costs assessed?costs collected for appropriate time period?
- If these costs were estimated from other research or source material, they should be referenced.
- Was there justification for any important costs or consequences that were not included?
- Sometimes the authors may admit that although certain costs or consequences are important, they were impractical (or impossible) to measure in their study.
- It is better that the authors state these limitations rather than ignore them. Other times, the costs are so small that it would not be worth the effort to measure them.

Costs...

- Protocol-driven costs are costs that occur because of the research protocol of a randomized, controlled trial that would not occur in everyday practice. For example, randomized, controlled trials for medications to treat stomach ulcers may include endoscopy
- Procedures at various intervals to determine the healing rate of the ulcers. In everyday practice, physicians commonly rely on patients' reports of symptoms (or lack of symptoms) to determine the effectiveness of the medication.
- Costs that are the same for all alternatives are also commonly excluded based on the argument that when conducting an incremental cost-effectiveness analysis, these costs would mathematically cancel out each other.

8. Relevant Outcomes: Were the Important or Relevant Outcomes Measured?

- Example 1, when comparing medications that reduce blood pressure, clinicians agree that the main outcomes are change in systolic and diastolic blood pressure.
- Example 1, When comparing medications that treat diabetes, is fasting blood glucose or hemoglobin A1C important (or are both important)?
- When comparing medications that treat asthma, there is more debate on what outcomes are most important to measure. Some clinicians may prefer to use forced expiratory volume (FEV) measurements.
- It is common in PE studies to use a measure - symptom-free days (SFDs), which are based on patient diaries or reports. When measuring outcomes, is the appropriate time period used?
- For acute medical problems, such as infections or influenza, following up patients until the problem is resolved (an episode of care) entails collecting information for every patient in a short time frame. Conversely, outcomes emanating from chronic conditions, such as high blood pressure and high cholesterol levels, may not be fully captured until many years have elapsed.
- It is important for the reader to evaluate whether the time period of data collection was appropriate for the clinical measures recorded.
- This is especially important when short-term clinical trial data are incorporated into pharmacoeconomic studies of chronic conditions.

9. Adjustment or Discounting: Was Adjustment Appropriate?

- If So, Was It Conducted? Was Discounting Appropriate? If So, Was It Conducted?
- If retrospective data were analyzed to assess resources used over a number of years, these costs should be adjusted, or standardized, to value resources at one point in time.
- In addition, if the costs or benefits were extrapolated more than 1 year out, the time-value of money must be incorporated into the cost estimates, using discount rates to calculate the present value.
- These are two different questions. It is possible that neither adjustment nor discounting is needed, that only adjustment is needed, that only discounting is needed, or that both are needed.

10. Reasonable Assumptions: Are Assumptions Stated and Reasonable?

- Pharmacoeconomic studies frequently require researchers to use estimates of costs or outcomes.
- Whenever estimates are used, there is a possibility that these estimates may not be precise (or universally agreed upon by the readers).
- These estimates may be referred to as assumptions.
- For example, authors may assume the cost of a laboratory test is $50, that patient adherence with a regimen will be 100%, discount rate is 3%.
- Assumptions should be stated explicitly. Authors may estimates without using the term "assumption," although using this term helps the reader differentiate between the values that were directly measured and the values that were estimated.
- Readers should ask themselves whether these estimates seem reasonable in the context of their practice or decision-making processes.

11. Sensitivity Analyses: Were Sensitivity Analyses Conducted for Important

- Sensitivity analysis allows to determine how the results of an analysis would change when "best guess" estimates, or assumptions, are varied over a relevant range of values.
- By using a plausible range of values for key assumptions, sensitivity analysis allows the researcher to examine the impact of these assumptions on the study conclusions.
- For example, if a researcher makes the assumption that the appropriate discount rate is 3%, this estimate might be varied from 0% to 6% to determine whether the same alternative would still be chosen within this range.
- If the same option or comparator were chosen for the full range of the sensitivity analyses, the analysis is said to be insensitive, or robust, to this range of values, thereby adding confidence in the study results.
- If the conclusions or choice of therapy changes on the basis of a plausible range of estimates, the results are deemed sensitive to this estimate, and readers should be aware of this when interpreting results.
  - Example , If the net savings of a clinic after 3 yr was $42,804 and if future costs/savings discounted at 3%, and $50,000 if discounting not conducted (0% discount rate). Either calculation resulted in positive net savings for the clinic; therefore, the choice of whether or not to implement the clinic was not affected by (insensitive to) the range of discount rates used (0% to 3%).

12. Limitations Addressed: Were Limitations Addressed?

- Because of practical restrictions, no study is ideal; therefore, the authors should mention the most important limitations of their study.
- Using retrospective data bases may increase the possibility of selection bias.
- Selection bias occurs when patients with certain characteristics are more likely to receive one treatment over another. Using a specific population may limit generalizability of results (see next critique question). Small sample sizes or missing data may limit statistical comparisons.
- There may be no data available on some cost or outcome values, which may require broad assumptions.
- It is better for the authors to address these limitations than to leave them unstated.

Bias

- Bias: Any such trend or deviation from the truth in data collection, analysis, interpretation and publication.

Type	Description
Recall bias	the researchers have to rely on the respondents' memories of the past
Selection bias	Research samples can sometimes under-represent certain people/groups, or over–represent others. (randomisation –best)
Observation bias	when participants in a study are aware that they are being observed by scientists and, either consciously or unconsciously, alter the way they act or the answers they give. Blind observation
Confirmation bias	may occur during the interpretation of study data when researchers, consciously or unconsciously, look for information or patterns in their data that confirm the ideas or opinions that they already hold.
Publishing bias	Studies with negative findings (i.e. trials in which no significant results are found) are less likely to be submitted by scientists or published by scientific journals because they are perceived as less interesting. These 'negative' results are as important for understanding a scientific topic as significant results are but they are less likely to be published

13. Appropriate Generalizations: Were Extrapolations Beyond the Population Studied Proper?

- If the study is based on data from a specific population of patients who may be atypical (e.g., in age, socioeconomic status, resource use) compared with the general patient population, the researchers should caution readers against generalizing, or extrapolating the results beyond the population studied.
- **Example**, results based on patients of long-term care facilities, the Veterans Administration, or state Medicaid may be different (in both costs and outcomes) from the results based on a population of ambulatory patients with private health care insurance.

14. Unbiased Conclusions: Was an Unbiased Summary of the Results Presented?

- Sometimes the conclusions seem to overstate or over extrapolate the data presented in the results section.
- Did the authors choose appropriate alternatives and use unbiased reasonable estimates when determining the results?
- In general, do you believe the results of the study? Does the study make sense?
- There may be is concern when studies sponsored by drug manufactures may be biased to show that their medication is cost-effective.
- Health plans that conduct pharmacoeconomic research may have an inclination to show a new treatment is not cost-effective and therefore will not be covered by the health plan.
- Assessment of the level to which research is biased versus unbiased should be based on the questions outlined above, not the funding source

END OF THE COURSE